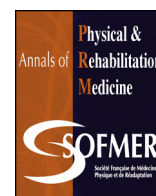




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## Letter to the editor

### Verrucous carcinoma on a chronic sacral pressure ulcer in a patient with meningomyelocele. Case report and review of the literature



#### 1. Case report

Mr G. was born in 1977 with meningomyelocele, operated in 1978, and presented complete AIS A T12 paraplegia and hydrocephalus with moderate mental retardation. His surgical antecedents were: ventriculoperitoneal shunt, augmentation enterocystoplasty and anti-reflux surgery in 1990, Salter pelvic osteotomy + Sharrard psoas muscle transfer in 1994.

In 2004 we managed the patient for the first time, for a sacral pressure ulcer, in the form of a cryptic and keratotic lesion. It was already a recurrence. In 2005, purulent discharge makes us practice an MRI, showing subcutaneous infiltration involving the sacrum (sacral osteomyelitis is suspected) and a cryptic zone in contact with the rectal wall.

A first musculocutaneous flap permitted a first biopsy of the sacral lesion in June 2005. Histological examination revealed chronic ulceration compatible with a diagnosis of pressure ulcer. The initial postoperative course was favourable, but at the beginning of 2006, purulent discharge on sacrum recurred, explained at MRI by persistence of a blind perineal fistula along the levator ani muscles and another fistula extending towards the coccyx (no signs of intestinal fistula). After two flap revisions in 2006 and 2007 allowing evacuation of large infected haematoma, closure of fistulas and after adapted dual-agent antibiotic therapy (against always the same germ: *Proteus mirabilis*), the patient has healed and regained his autonomy. All histological examinations were compatible with a chronic wound with no sign of malignancy.

No complication was observed during a 3-year period of outpatient follow-up. An annual follow-up CT urography incidentally revealed a sacral mass (Fig. 1). MRI confirmed the presence of an infiltration with a paraspinous collection extending from L3 to the sacrum associated with sacral bone destruction, suggesting an infectious process (Fig. 2).

The patient was admitted to hospital for a infected stage 3 sacral pressure ulcer and new fistulas. He was malnourished, had chronic anemia and signs of sepsis. In a multidisciplinary consultation meeting (MCM), we decided to practice excision of the pressure ulcer and exploration of the fistulas (no intestinal fistula founded), one on the right hip. Histological examination revealed the presence of epidermal cysts with no histological signs of malignancy. Triple agent antibiotic therapy was initiated.

An MRI performed in February 2011 showed no improvement, so the patient was reoperated for an oncologic-like resection including: sacrum, right sacro-iliac joint and the right Sharrard psoas muscle transfer and resection of the head and neck of the

right femur due to the suspected infectious process. The macroscopic appearance evoked secondarily infected epidermoid cyst. Histological examination showed a squamous cell proliferation with multiple large lobules and marked inflammatory infiltrate, sometimes presenting features of granulation with several sites of bone metaplasia. The diagnosis was impossible to confirm in view of the fragmented nature of the sample, it could have been a pseudocarcinomatous epidermal hyperplasia or a verrucous carcinoma.

The postoperative course was initially uneventful, but recurrence of the purulent discharge was observed in May 2011. Pelvic MRI (Fig. 3) showed reactivation of the purulent collections and inflammatory signs, accompanied by blind fistulous tracks in the right buttock and left pararectal region.

A third operation was decided following a multidisciplinary consultation at the end of May 2011, due to the poor local improvement, the MRI findings and the highly septic general status. A more extensive resection was performed: resection of the right psoas muscle, revision of the femoral head-neck resection, total resection of L5. Histological examination of the resection specimens was unable to clarify the differential diagnosis between epidermoid cyst and verrucous carcinoma. Negative-pressure wound therapy was initiated but in July 2011, MRI demonstrated important worsening (Fig. 4). Debridement surgery was performed with cleaning, drainage, and insertion of absorbant dressings into the posterior collections.

Histological examination of these biopsies confirmed the presence of verrucous carcinoma. We observed a highly differentiated squamous cell proliferation with a verrucous architecture, infiltrating the skin and bone (Fig. 5).

A total of 4 radical resection surgical procedures on the pelvis were performed over a period of one year with persistence of the tumour (Figs. 6 and 7). The multidisciplinary consultation meeting decided to withhold any further surgery and, in view of the negative staging assessment, only analgesic radiotherapy was proposed, but finally not performed as the patient did not experience any pain as the zone was situated below the level of the spinal cord lesion. Only local wound care was continued. Antibiotics were stopped 6 months after the last operation (lack of efficacy and poor tolerability). As the patient's general state had deteriorated, priority was given to ensuring his comfort in the context of palliative care. He died in 2013 of a major deterioration of his general condition.

#### 2. Discussion

Mr G. developed a verrucous carcinoma, or cuniculatum carcinoma (a very highly differentiated squamous cell carcinoma) on a chronic pressure ulcer, consisting in a Marjolin's ulcer.

Historically, the relationship between burn scars and skin carcinoma was first recognised by Jean Nicolas Marjolin in 1828

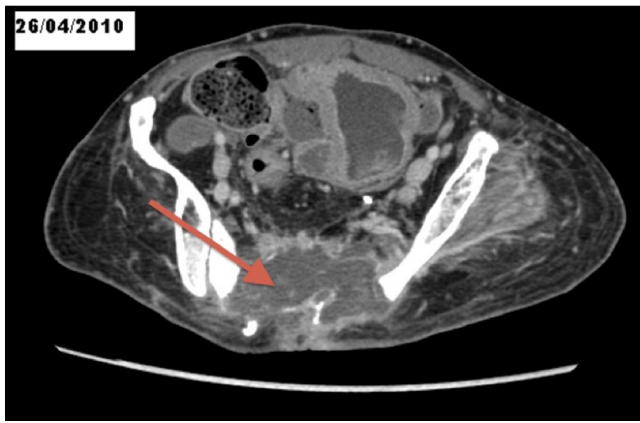


Fig. 1. CT, April 2010: paraspinal collection.

[1]. The English surgeon, Caesar Hawkins was the first to confirm malignant transformation of burn scars and chronic wounds [2]. In 1903, Da Costa coined the term “Marjolin’s ulcer” to describe skin tumours arising in chronic ulcers of various origins [3] and this generic term is still used.

The case presented here is particular as the patient developed multiple pressure ulcers arising from persistence of a hyperkeratotic and cryptic zone contiguous with the spina bifida scar. The subcutaneous and bony infiltration of these ulcers was initially mistaken for pelvic osteomyelitis on the basis of negative histological examinations. Verrucous carcinoma often mimic a local infection because they are very secreting. The diagnosis was delayed because of the high differentiation. Retrospectively, the slides already showed the presence of carcinoma in 2010. Local

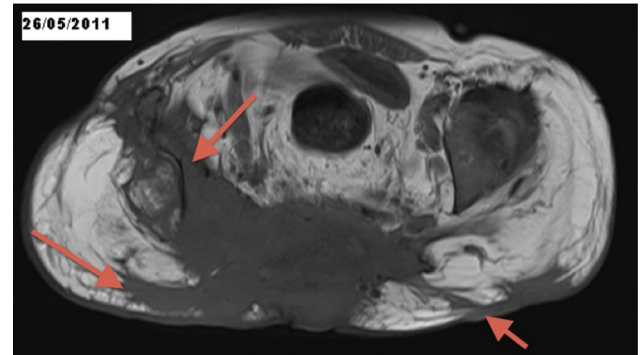


Fig. 3. MRI, May 2011: gluteal fistulas, extending to the right hip.

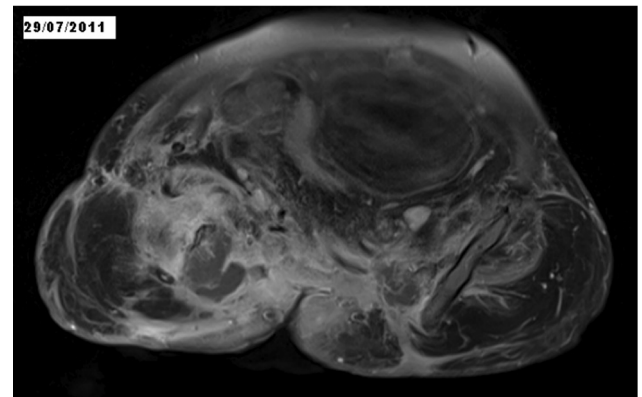


Fig. 4. MRI, July 2011: Collections extending to both hips.



Fig. 2. MRI, August 2010: Sacral bone destruction.

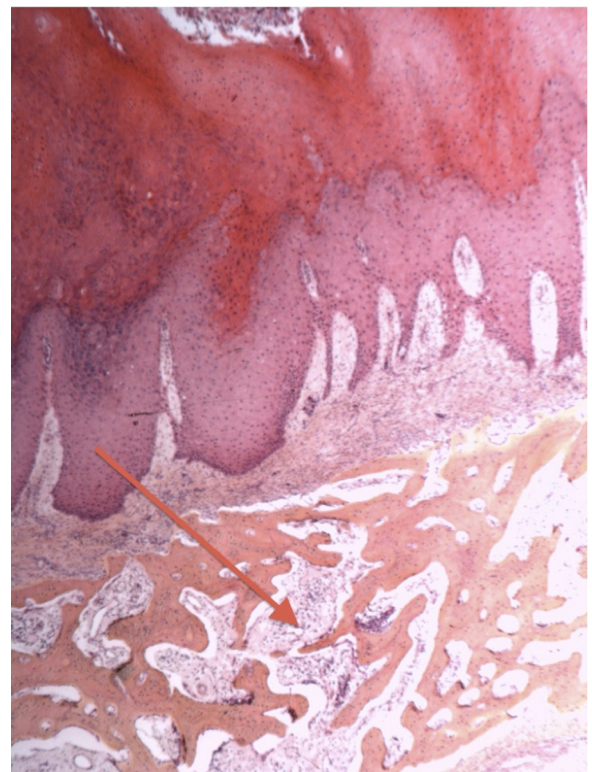


Fig. 5. Histology, September 2011: well differentiated squamous cell carcinoma with multiple, large lobules lined by squamous cell epithelium with no marked architectural disorganization or cytonuclear atypia. Clearly visible extension to bone.

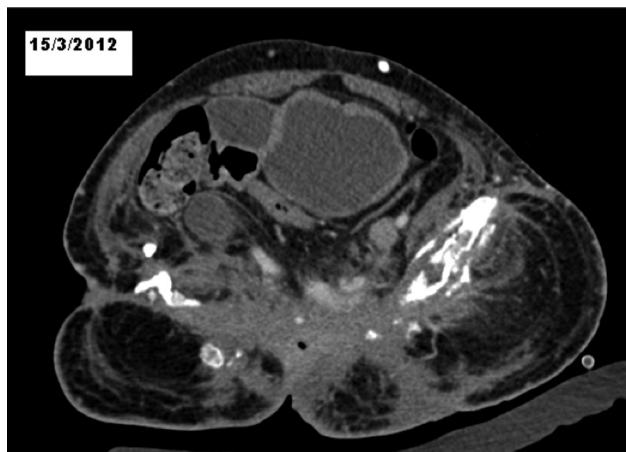


Fig. 6. CT, January 2012: Destruction of the ilium.

infiltration was so severe that even successive oncologic-like resections failed to cure this disease (in contrast with a similar case [4] published in 2004 by Peterson in a repeatedly operated spina bifida patient).

In literature, a study published in 2002 in the J Spinal Cord Med [5], based on the follow-up of 10,000 spinal cord injury patients, showed that 5 patients developed Marjolin's ulcer, always associated with a fatal outcome, probably as a result of the delayed diagnosis. Similarly, in this case published by Lack in 2010 [6], we can see the very high local invasive potential of this disease.

Several authors have also published case reports concerning the development of squamous cell carcinoma specifically at the dysraphic zone of patients with meningocele, operated [4] or nonoperated patients [7–12], suggesting the importance of the primary disease in the subsequent development of cancer. Peter Nthumba, in 2010 [13], reviewed all of the various theories proposed to explain the development of Marjolin's ulcer and reported two other clinical cases of malignant transformation of sacral pressure ulcers in spina bifida patients [14], emphasizing the importance of close follow-up of these patients. Patient therapeutic education is also essential [15].

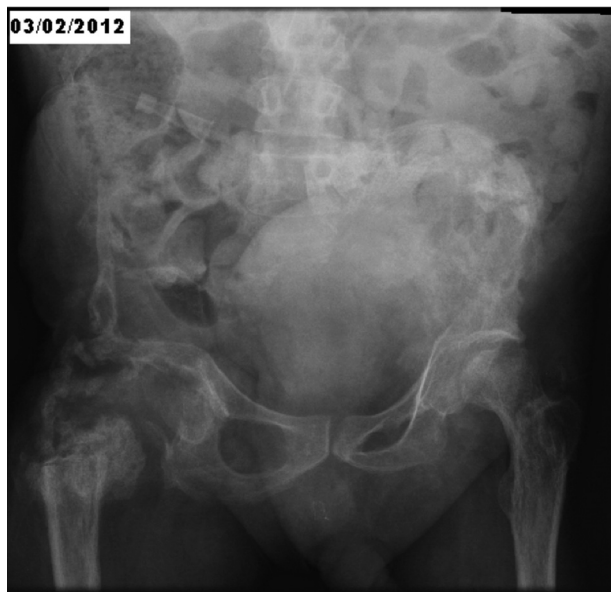


Fig. 7. March 2012: AP view of the pelvis showing loss of the normal appearance of the iliac bones and spine as far as L4.

Factors of poor prognosis of Marjolin's ulcers are [13]: Marjolin's ulcers present for more than 5 years, situated on the lower limbs and trunk, arising on a pressure ulcer (better prognosis if burn), more than 2 cm in diameter, infiltration with metastasis and recurrence, poorly differentiated cancer, absence of T lymphocytes around the ulcer, invasion to a depth of more than 4 mm. The case reported here presented 6 of these 8 factors of poor prognosis.

In pathophysiology, several theories have been proposed to explain the development of Marjolin's ulcer on chronic wounds [13]: toxins released by damaged tissues lead to cell mutations; poor lymphatic drainage would allow tumour cells to proliferate; p53 gene mutations (tumor suppressor gene) would induce a susceptibility to the development of skin cancer...

In spina bifida patients, two other theories are interesting:

- chronic irritation and repeated trauma during re-epithelialisation can induce malignant transformation (e.g. to explain malignant transformation of nonoperated meningocele);
- invagination of epithelial cells into the dermis would induce a foreign body reaction and a disorder of the regeneration process (this theory would be applicable to patients with a dysraphism, even when operated)

In this case, what was the real origin of his cancer: simply a Marjolin's ulcer arising on a chronic wound, or did the verrucous carcinoma occur in this patient in particular because of the presence of spinal dysraphism or invagination of epidermal tissues into the dermis at the time of the meningocele repair surgery?

### 3. Conclusion

Dysraphism *per se* may therefore constitute a supplementary risk factor for the development of carcinoma in the dysraphic zone. The association between spina bifida and the development of Marjolin's ulcers must be taken into account in the management of these patients, who require very close follow-up [13]. Any wound or fistula occurring over the dysraphic zone must not be ignored whenever it becomes chronic, recurrent, or presents signs of transformation [3].

### Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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